A+

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/948,149	10/09/1997	BRIAN M. FENDLY	P1053R2	6683

24510 7590 05/26/2004

PIPER MARBURY RUDNICK & WOLFE LLP
STEVEN B KELBER
1200 NINETEENTH STREET, NW
WASHINGTON, DC 20036-2412

EXAMINER	
SWARTZ, RODNEY P	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/948,149	FENDLY ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25February2004, 23March2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-40 and 42-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-40,42-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection, received 25February2004. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25February2004 has been entered.

2. Applicants' Amendment, received 25 February2004, is acknowledged. New claims 63 and 64 have been added.

3. Applicants' Supplemental Amendment, received 23March2004, is acknowledged. Claims 32, 34, 42, 58, and 64 have been amended.

4. Claims 28-40 and 42-64 are pending and under consideration.

Rejections Maintained

5. The rejection of claims 28-31, 37-38, 40, 56, and 57 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991) is maintained for reasons of record.

Applicants argue that the antibodies 7F3 and 7C2 were no publically distributed or publically available more than one year prior to October 18, 1996, the priority filing date of the instant application.

The Examiner has considered applicants' argument, but does not find it persuasive in light of the dated MTA submitted by applicants. The MTA is dated 1993, more than one year prior to October 18, 1996.

Applicants argue that the monoclonal antibodies are not available to just "anyone" but only to researchers who obtained prior approval from Genentech for their research plan and complied fully with the Materials Transfer Agreement. This constitutes a "threshold requirement" concerning the complete control that Genentech exercised over the material. Applicants argue that the Examiner oversimplified and mischaracterized the availability of the materials by stating that "anyone" can get the materials simply by agreeing to the restrictions of the MTA. Applicants argue that the Examiner ignored the Declaration of Gail Phillips which stated that an investigator's research plan had to be first approved by Genentech.

The examiner has considered applicants' argument, but does not find it persuasive. If the reference describes the invention so that one can reproduce it, or if the required antibody is in public use in the method, or can be obtained by the public (which it can be as long as the requester is willing to meet the MTA requirements), then the prior art meets the requirements of 35 U.S.C. 102(b) and 35 U.S.C. 103(a).

Applicants argue that an outside investigator operating under the Genetech MTA would have no freedom whatsoever to use the provided materials outside of the restrictions of the MTA or to disclose or distribute those materials to a third party.

The examine has considered applicants' argument, but does not find it persuasive because the issue in not whether the material is disclosed or distributed to a third part, but that the material is accessible to the public, i.e., directly from Genentech. As stated in prior rejections, the materials are available to any investigator who agrees to the restriction of the Genentech MTA.

6. The rejection of claims 28-31, 37-38 and 40 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) is maintained for reasons of record.

Applicants arguments are those put forth in the rejection, section **5**, *supra*. The examiner has considered applicants, but does not find them persuasive for the same reasons put forth *supra,* section **5**.

7. The rejection of claims 32-36, 39, and 58 under 35 U.S.C. 103(a) as being unpatentable Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991), or Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993), in view of Fendly et al (*Cancer Research*, 50:1550-1558, 1990), Deshane et al (*J. Invest. Med.*, 43(Suppl 2):328A, 1995), and further in view of Senter et al (U.S. Pat. No. 4,975,278) is maintained for reasons of record.

Applicants arguments are those put forth in the rejection, section **5**, *supra*. The examiner has considered applicants, but does not find them persuasive for the same reasons put forth *supra,* section **5**.

8. The rejection of claims 42-55 and 59-62 under 35 U.S.C. 103(a) as being unpatentable Shepard et al (*J. Clinb. Immunol.*, 11(3):117-127, 1991), in view of Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993) and Fendly et al (*Cancer Research*, 50:1550-1558, 1990), and further in view of Deshane et al (*J. Invest. Med.*, 43(Suppl 2):328A, 1995) and Senter et al (U.S. Pat. No. 4,975,278) is maintained for reasons of record.

Applicants arguments are those put forth in the rejection, section **5**, *supra*. The examiner has considered applicants, but does not find them persuasive for the same reasons put forth *supra,* section **5**.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 63 rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991).

Claim 63 is drawn to a method for inducing cell death comprising exposing a cell which overexpresses ErbB2 to an effective amount of an isolated antibody that binds to an epitope on ErbB2; wherein said isolated antibody induces cell death.

Claim 63 utilizes the open language "comprising" in delineating the methods steps. Such language encompasses induction of apoptosis which is taught in the instant specification as one of the mechanisms by which the claimed antibody induces cell death, but the scope of the claim is not restricted only to apoptosis, nor is the language restricted as to the use of other reagents, such a complement, phagocytic cells, cytotoxic drugs, or growth inhibitory agents, in addition to the antibody. The specification teaches that antibodies 7C2 and 7F3 bind to Domain 1 of ErbB2 and that antibody 4D5 binds to ErbB2, but not to Domain 1.

Shepard et al teach a monoclonal anti-HER2 antibody ($d5) which: a) inhibits the growth of SKBR3 breast tumor cells in cell culture by 66% (Abstract; Table II); b) enhances the ensitivity of SKBR3 cells to cisplatin (Figure 5); and c) enhances the sensitivity of SKBR3 cells to TNFα (Figure 4). Shepard et al also teach monoclonal anti-HER2 antibodies 7C2 and 7F3 which bind to Domain 1 of ErbB2 (Fig. 2; page 119, section **Derivation of muMab 4D5**) and which inhibit SKBR3 proliferation by 21% and 38% respectively (Table II).

In the absence of evidence to the contrary, antibodies 7C2, 7F3, and 4D5 in the instant application are the same antibodies in the cited references because applicant Brian M. Fendly, of Genentech, Inc., is also the co-author on the cited reference which also lists Genentech, Inc. as the address of correspondence. Both the instant application and the cited reference also teach that the antibodies bind to ErbB2. Therefore, the antibodies are the same because: 1) same laboratory, 2) same author/applicant, 3) same laboratory designation for the antibodies, 4) same procedures for producing antibodies, and 5) same reactivity, i.e., bind to ErbB2(HER2).

Since the same laboratory designation is utilized in both the instant application and the cited reference, from the same laboratory, the properties of antibodies 7C2, 7F3, and 4D5 in the cited reference are inherent concerning; 1) binding to Domain 1 of ErbB2, 20 binding another Domain, and 3) 5-50 fold induction of annexin binding.

11. Claim 63 rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993).

Claim 63 is drawn to a method for inducing cell death comprising exposing a cell which overexpresses ErbB2 to an effective amount of an isolated antibody that binds to an epitope on ErbB2; wherein said isolated antibody induces cell death.

Claim 63 utilizes the open language "comprising" in delineating the methods steps. Such language encompasses induction of apoptosis which is taught in the instant specification as one of the mechanisms by which the claimed antibody induces cell death, but the scope of the claim is not restricted only to apoptosis, nor is the language restricted as to the use of other reagents, such a complement, phagocytic cells, cytotoxic drugs, or growth inhibitory agents, in

addition to the antibody. The specification teaches that antibodies 7C2 and 7F3 bind to Domain 1 of ErbB2 and that antibody 4D5 binds to ErbB2, but not to Domain 1.

Lewis et al teach monoclonal anti-HER2 monoclonal antibodies, e.g., 4D5, 7C2, and 7F3, which inhibit human tumor cells such SKBR3 (Table 2) and mediate antibody-dependent cellular cytotoxicity (Figure 4).

In the absence of evidence to the contrary, antibodies 7C2, 7F3, and 4D5 in the instant application are the same antibodies in the cited references because applicant Brian M. Fendly, of Genentech, Inc., is also the co-author on the cited reference which also lists Genentech, Inc. as the address of correspondence. Both the instant application and the cited reference also teach that the antibodies bind to ErbB2. Therefore, the antibodies are the same because: 1) same laboratory, 2) same author/applicant, 3) same laboratory designation for the antibodies, 4) same procedures for producing antibodies, and 5) same reactivity, i.e., bind to ErbB2(HER2).

Since the same laboratory designation is utilized in both the instant application and the cited reference, from the same laboratory, the properties of antibodies 7C2, 7F3, and 4D5 in the cited reference are inherent concerning; 1) binding to Domain 1 of ErbB2, 20 binding another Domain, and 3) 5-50 fold induction of annexin binding.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claim 64 rejected under 35 U.S.C. 103(a) as being unpatentable over Shepard et al (*J. Clin. Immunol.*, 11(3):117-127, 1991), or Lewis et al (*Cancer Immunol. Immunother.*, 37:255-263, 1993), in view of Fendly et al (*Cancer Research*, 50:1550-1558, 1990).

Claim 64 is drawn to a method for inducing cell death comprising exposing a cell which overexpresses ErbB2 to an effective amount of an isolated antibody that binds to an epitope on ErbB2; wherein said isolated antibody induces cell death; wherein said second anti-ErbB2 antibody does not bind to an epitop[e on erbB2 to which antibody 7C2 binds.

Claim 64 utilizes the open language "comprising" in delineating the methods steps. Such language encompasses induction of apoptosis which is taught in the instant specification as one of the mechanisms by which the claimed antibody induces cell death, but the scope of the claim is not restricted only to apoptosis, nor is the language restricted as to the use of other reagents, such a complement, phagocytic cells, cytotoxic drugs, or growth inhibitory agents, in addition to the antibody. The specification teaches that antibodies 7C2 and 7F3 bind to Domain 1 of ErbB2 and that antibody 4D5 binds to ErbB2, but not to Domain 1.

Shepard et al teach a monoclonal anti-HER2 antibody (4d5) which: a) inhibits the growth of SKBR3 breast tumor cells in cell culture by 66% (Abstract; Table II); b) enhances the ensitivity of SKBR3 cells to cisplatin (Figure 5); and c) enhances the sensitivity of SKBR3 cells to TNFα (Figure 4). Shepard et al also teach monoclonal anti-HER2 antibodies 7C2 and 7F3 which bind to Domain 1 of ErbB2 (Fig. 2; page 119, section **Derivation of muMab 4D5**) and which inhibit SKBR3 proliferation by 21% and 38% respectively (Table II).

Lewis et al teach monoclonal anti-HER2 monoclonal antibodies, e.g., 4D5, 7C2, and 7F3, which inhibit human tumor cells such SKBR3 (Table 2) and mediate antibody-dependent cellular cytotoxicity (Figure 4).

Fendly et al teach the production and characterization of the monoclonal anti-HER2 antibodies utilized by Shepard et al and Lewis et al (Abstract; page 1550-1552, section **Materials and Methods**).

Thus, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to use anti-HER2 antibodies which bind to various epitopes on ErbB2, such as 4D5, 7C2, and 7F3 as taught Shepard et al, Lewis et al, and Fendly et al to induce cell death in a cell which overexpresses ErbB2.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claim 64 is rejected under 35 U.S.C. 112, second paragraph, because the claim recites the limitation "the method of claim 63 wherein said second anti-ErbB2 antibody" in line 1.

There is insufficient antecedent basis for this limitation in the claim because claim 63 does not recite a second antibody.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Thursday from 5:30 AM to 4:00 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F. Smith, can be reached on (571)272-0864.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

May 18, 2004